

Graduation thesis.

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AN INVESTIGATION INTO THE CHARACTER OF SMALL-POX,  
AND AN ACCOUNT OF A NEW TREATMENT SUGGESTED  
THEREBY .

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An Investigation of the Character of Small-pox, and an  
Account of a New Treatment Suggested thereby.

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With one exception the acute exanthemata usually run normally a more or less rapid uncomplicated course. There is first the invasion of the body by the specific organism of the disease, followed in regular order by the period of incubation, during which the organism multiplies and the patient suffers from general malaise, then the fastigium, in which the constitutional disturbance is at its highest and the particular symptoms of the disease most marked, this in turn is followed by "defervescence", when the temperature falls, the symptoms abate, and the patient, unless complications supervene, is on the road to recovery. Not only has the patient recovered, but he has also acquired, for a shorter or longer period, an immunity against the disease from which he has been suffering. Complications, such as pneumonia in measles, are not, in all probability, due directly to the organism causing the disease, they only occur in a certain percentage of the cases, and cannot properly be assumed to be part of disease they follow with more or less frequency.



Small-pox at first follows the ordinary course of the exanthemata; there are the periods of invasion, incubation, the fastigium, and defervescence. But defervescence, and herein small-pox apparently differs from all the other acute exanthemata, is of very short duration and is immediately followed by what is termed the "secondary fever" of small-pox. In discussing the disease with a friend of mine, Dr. Reid, this extraordinary difference between small-pox and the other exanthemata struck us very forcibly, and subsequent consideration and investigation have convinced me that in point of fact the difference is apparent rather than real, <sup>and</sup> ~~and~~ that the pathological conditions ~~that~~ we term small-pox are in reality two separate and distinct diseases. The first, small-pox proper, comes to an end with the fall of the temperature on the fourth or fifth day, the subsequent illness, with its rise of temperature and characteristic symptoms, is, correctly speaking, not small-pox but sapraemia. The small-pox organism, moreover, beyond its predisposing action, plays no part whatever in the pyrexia and other subjective symptoms of the secondary fever.

The arguments that I shall adduce will, I think, carry conviction that the foregoing is a correct

statement of the case.

In the first place let us compare the character of the symptoms in the initial stage, which I shall term small-pox proper, with that of the second which goes by the name of the secondary fever. The principal symptoms of smallpox proper are malaise, headache, vomiting, with marked pain in the shoulders and back, and sometimes acute delirium; those of secondary fever are sordes of the teeth and gums, foetid breath, muttering delirium, muscular tremors, and a general typhoid condition. It cannot fail to strike the observer that the latter are totally different from those of small-pox proper, and, which is very important, must therefore be due to entirely different organisms. To deny this would be assume, against all evidence and presumption to the contrary, that the specific organism has the power, during its life in the body, of so changing its character and properties as to give rise to a totally different set of subjective symptoms. Such a theory cannot for a moment be entertained. There is moreover stronger evidence than presumption that the organisms of the two stages are different; there is evidence of fact. The organism of small-pox

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\* "Infectious Diseases.", Goodall and Washbourn, p.207.

has not, it is true, been satisfactorily identified, there can be little doubt, however, that it is present in the papules and early vesicles of the rash, repeated examination of these have, on the other hand, failed to discover in them any pyogenic organisms. Pyogenic organisms, however, are present in large quantity in the later vesicles and pustules.<sup>x</sup> I have myself found staphylococci pyogenes albus and aureus, others have demonstrated the presence of the streptococcus pyogenes and other saprophytes. It may be urged that the small-pox organism is also present in these later stages, this is probably true, but the mere fact of its presence does not warrant the inference that therefore it plays a pathogenic part in the secondary fever. There is ample evidence that the specific organism of a disease persists in the body long after it has ceased to give rise to any symptoms: an example of which is seen in diphtheria, where the Klebs-Loeffler bacillus has been found in the throats of patients months after they have quite recovered from the disease.

This, however, does not exhaust the evidence in favour of the stages being distinct diseases.

I have stated that in the acute exanthemata

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<sup>x</sup>"Infectious Diseases", Goodall and Washbourn, p.207.

the patient, after the fall of the temperature, has acquired for a shorter or longer period an immunity against the particular disease he may have been suffering from. Various theories to account for the phenomenon of acquired immunity have been brought forward, but, so far as I am aware, with none is it consistent to assume, (as we must assume if we imagine the small-pox organism to play a part in the secondary fever) that, after the fall of temperature and immunity is acquired, the organism undergoes a rejuvenescence so as to again react deleteriously on the tissues of the body. And there is also evidence ~~that~~ that the stage at which immunity is acquired in small-pox is when the rash appears and the temperature falls. Proof of this may be found in the study of vaccination:- "In the report of the Committee of the Clinical Society on Incubation will be found notes of twenty-two cases in which successful <sup>vaccination</sup> or revaccination was performed at times varying from thirteen days before the outcome of the eruption of small-pox up to, in one case, the very day of its appearance. In this case successful vaccination was performed a few hours before the outcome of the smallpox eruption; but this appears to be quite an exceptional occurrence. During



the eruptive stage of small-pox, during convalescence, and for a long period afterwards, successful vaccination is impossible.<sup>x</sup>"

If therefore the patient is protected against reinfection of the disease from the outside, it is only reasonable to assume that he is equally protected or immune from auto-reinfection. (In the foregoing argument I have assumed that vaccinia is merely a modified form of small-pox. I am aware that there are some who still maintain the contrary, but the proofs, which, not to unduly prolong my main argument I have given in an appendix, appear to me conclusive on the subject.)

Still further evidence is obtainable from vaccination as to the distinctness of the two stages. In the first place in pure vaccine lymph there are no pyogenic organisms, this has been demonstrated by many observers and is dealt with at length in the Milroy Lectures for 1898. In this work also occurs the following statement:- "If the vaccine vesicle of a healthy child or calf be carefully opened at an early stage with all aseptic precautions, and a droplet of the lymph which exudes from it be submitted to bacteriological examination, it may not unfrequently be found, as Klein has also demonstrated, that such lymph is absolutely pure

<sup>x</sup> "Infectious Diseases," Goodall and Washbourn, p225.  
 "Vaccination", the Milroy Lectures, S.M. Copeman 1898.

in the sense that it contains no micro-organisms that will grow on ordinary culture media. Yet it is perfectly efficient as vaccine." <sup>x</sup>

It will be granted, I think, that the arguments I have submitted, -the difference in symptoms, the phenomenon of immunity, and the bacteriological relations, -are sufficient to prove that the initial rise and the secondary fever are two separate and entirely distinct diseases: that the organism of small-pox has no direct causal relation to the secondary fever and its symptoms; that the latter are entirely due to ordinary pyogenic organisms; and finally that although the latter admittedly follow the small-pox proper with great regularity, they are as a matter of fact accidental.

If, however, the above conclusion lead to no practical benefit, this thesis would be of little beyond academic interest. This is not the case, and I shall now endeavour to show how an appreciation of the above facts indicates a new method of treatment of small-pox which, as practised by myself has been perfectly successful, and which will, I believe, be found in all cases to be immeasurably superior to any treatment yet published.

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<sup>x</sup> "Vaccination", S.M.Copeman, p.106.



It is first necessary to consider why, if the stages are so distinct as I affirm, the secondary fever should appear in small-pox with such regularity.

The following appears to me a perfectly logical explanation of the various phenomena that occur in a case of small-pox. There is first the invasion of the body by the small-pox organism, the tissue principally affected is the rete Malpighii where presumably the organism is deposited. This being of the nature of an irritant there is local reaction against it with the usual exudation of serum and leucocytes. The result of this exudation is to exert such pressure on the skin immediately over the vesicles as to deprive it of nutriment and <sup>there is</sup> consequent loss of vitality. We have therefore in the vesicular stage numerous small areas of dead tissue on the surface of the body. The vesicles, it must be borne in mind, do not in their early stages contain any pyogenic bacteria. In their later stages they contain numerous pyogenic organisms. The explanation of this must be that these areas of dead tissue form a suitable pabulum for the numerous saprophytic organisms that are always present in the atmosphere. I may be met here possibly with the objection that these organisms may gain access to the

vesicles from within and not from the outside. To this I would reply that there is no evidence of such being the case, moreover, if it were so we should expect to find pyaemic abscesses very frequently, whereas they are, as a matter of fact, very rare in small-pox. Still more conclusive to my mind, however, is the following: I thoroughly disinfected a papule and then kept it covered with antiseptic dressing for five days; at the end of that period I inoculated some blood serum with the contents of the vesicle with the result that there was no growth whatever, whereas blood serum inoculated with the contents of another vesicle, on the same patient, that had not been so protected gave a copious growth of staphylococcus pyogenes albus and aureus. The pus in the one vesicle was septic, that in the other nonseptic.

It is essential to an appreciation of my argument that there should be a clear understanding of the meaning I attach to the expression "nonseptic pus." I trust therefore I may be pardoned for discussing the character of pus somewhat in detail.

It was at one time held that all pus formation was due to the presence of micro-organisms, this has since been disproved. "It has been demonstrated

by the experiments of Grawitz, De Bary, and others that certain chemical substances, which act as local irritants when brought in contact with the tissues, may induce pus formation quite independently of micro-organisms: nitrate of silver, oil of turpentine, and strong liquor ammoniae have been shown to possess this power. And it has been demonstrated by the recent experiments of Buchner that sterilized cultures, of a long list of different bacteria -seventeen species tested, give rise to suppuration when introduced into the subcutaneous tissues".<sup>x</sup> Now the pus formed in such cases as the above consists of what I term "nonseptic pus": that is to say pus which is of itself incapable of causing septic absorption, for it contains no septic organisms. It consists merely of the leucocytes and serum exuded by the tissues of the body in the process of reaction against an irritant. If, however, septic organisms gain access to this pus it is rapidly converted into septic pus from which poisonous products are absorbed, giving rise to the characteristic symptoms of septic poisoning.

The above is the explanation of what takes place in the septic pustulation of the vesicles of small-pox, the nonseptic pus becomes infected with septic organ-

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<sup>x</sup>"Bacteriology", Sternberg, p.224.

isms, and the symptoms of the secondary stage are purely and simply those of septic poisoning which we should naturally expect therefrom.

From the foregoing, the treatment that I propose will be apparent, it is so to protect the vesicles as to prevent their becoming infected with saprophytic organisms. If this is done there will be no septic suppuration and consequently no secondary fever.

Except in the forms of small-pox known as haemorrhagic and black small-pox death always occurs in the secondary fever, it is of course obvious that the treatment I suggest will have no effect on the former, in all other forms, however, I am convinced, that provided this antiseptic treatment is sufficiently and thoroughly applied a fatal termination will nearly always be prevented. There is also another advantage this is, that owing to the prevention of suppuration and consequent prevention of the destruction of the deeper layers of the skin, there is absolutely no pitting or disfigurement.

The method of applying the aseptic treatment that I have adopted was as follows:

The hair and beard on the face <sup>is clipped</sup> or shaved as close as possible, he is then put in a bath of 1 in 100 solution of izal, special attention being paid to the

face and head. He is then put into bed between sheets previously soaked in izal and dried. The whole body is then swathed in several thicknesses of izal gauze, each limb being freely mopped with izal solution before being covered and bandaged whilst wet. Iodoform is freely sprinkled over any parts that threaten to be particularly affected by the rash. The head and face is mopped at least three times with izal solution and finally dusted over with iodoform, a large sheet of eight folds of izal gauze is then allowed to fall all over the head and shoulders and the whole bandaged closely down on to the skin, it is advisable then to run a few stitches through the bandages to prevent slipping. holes are then cut for the eyes, nose and mouth, and the openings thus made carefully packed round the edges with izal cotton-wool.

Once the patient has been bandaged there is no need to remove the dressings, unless any of them become displaced when the skin is again carefully disinfected and the bandage replaced.

I attach no importance to the particular antiseptic dressing that is used, I employed izal simply because it is nonpoisonous, clean, and patients do not seem to mind the smell of it.

Since thinking out the above treatment, five

patients have come under my charge at the Portsmouth Small-pox Hospital. All have been treated in the manner I have described, and all have made perfect recoveries. The patients were:

Harry George, male, aet. 44, vaccinated in infancy only, 2 marks, very slight vevation. The attack was of a severe discrete character, the part principally affected was the forehead on which there were about 60 papules.

Alice George, female, aet. 32, (wife of the above), vaccinated in infancy, 2 marks; revaccinated on March 7th., eleven days before the appearance of the first symptoms, this revaccination took and the vaccinia and variola ran their course concurrently. It was a mild discrete case. An interesting point was the fact that this patient was confined after she had been in Hospital fifteen days. The confinement was at full time and perfectly normal in character. The baby, a girl, was quite healthy and has not shown any trace of the disease.

Robert Wiseman, male, aet. 24, vaccinated in infancy, two marks. A confluent case.

John Templeton, male, aet. 32, vaccinated in infancy only, two marks. A semiconfluent case.

Harry Turner, male, aet. 19, vaccinated in infancy



only, three marks. A confluent case.

It is unnecessary, as I have appended the charts of all the above cases to discuss each separately. The disease in every one followed exactly the course that I had anticipated. In none was there any secondary fever, moreover there were no symptoms whatever of septic poisoning; after the fall of the initial temperature, all the patients stated that they felt quite well and comfortable. They slept well, there was no headache, their appetites and digestion were good, in most cases they were put on ordinary diet within a few days of admission to the Hospital. In no case was there any subjective symptom of any pathological condition.

The dressings were kept on till about the fourteenth or fifteenth day, though in the case of Alice George, which was a very mild one, they were removed on the ninth. When they were removed it was found that a large proportion of the scabs had separated, leaving the skin beneath slightly injected but healthy and unpitted. The scabs were of a light yellowish brown colour instead of the dirty brown or black colour usually seen in small-pox, those that still remained after the removal of the dressings rapidly separated with bathing.

During the whole course of the disease there was not, even in the worst cases, the least foul odour from the skin, and, as I have stated before, bacteriologic-al examination of the pustules failed to discover the presence of any septic organisms. In the worst case, that of Robert Wiseman, the breath, however, was slightly foul. This I accounted for by the number of pustules in the mouth and back of the pharynx; it was noticed on the 9th, 10th, and 11th days. There was evidently, however, not enough septic absorption from these to cause any constitutional disturbance.

I attach great importance to the necessity of exercising the greatest care to keep the face aseptic. <sup>h</sup> This is not so much on the ground of the prevention of pitting, but because the effects of septic absorption are always more severe from the face than from other parts of the surface of the body.

In the case of Robert Wiseman I mentioned that a foulness of the breath was noticed on three days. This suggests to me that possibly in those cases of small-pox in which there is extensive suppuration of the mucous membrane of the mouth, pharynx, trachea and bronchi, we may fail to altogether prevent the secondary fever, owing to the difficulty of keeping these parts aseptic. Antiseptic gargles and inhal-

ations would doubtless be of service, but I do not at present see how their application can be made continuous or thorough enough to effect complete asepsis. Possibly antistreptococcus serum or some similar antitoxin may be found of use but I cannot speak of these from experience.

I trust I have now shown that the treatment of small-pox I recommend is a successful one, that it is moreover reasonable and based on sound scientific principles.

It is my firm belief that in the recognition of the true character of small-pox and its relationship to the secondary fever, lies the only means of being able to treat the disease with any hope of success. Up to the present the best treatment has been of little avail; in the future, if the treatment I have described, or possibly some modification of it, be adopted, I am convinced it will lead to complete prevention of disfigurement, and to, what is of far greater importance, a considerable saving of life.

I had intended, in addition to the views I have expressed on the relationship between vaccinia and small-pox, to have added a chapter on immunity, showing that under none of the theories yet promulgated could the organism of small-pox be conceived to play any

active part in the secondary fever. As this point is not, however, essential to my argument, and my paper has already reached considerable length, I have decided to omit further reference to it; I will only state that if anyone investigates the question ~~they~~ will, I think, undoubtedly come to the conclusion I have indicated.

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## APPENDIX 1.

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## The RELATIONSHIP between SMALL-POX and VACCINIA.

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That vaccinia undoubtedly protects the subject, for a longer or shorter period, against small-pox must be granted. Still further, the protection is mutual, not only does vaccination protect against small-pox, but an attack of small-pox equally protects the subject against vaccination. But for the specific organism of one disease to protect the subject against the specific organism of another disease is a thing unknown in pathological science. There are therefore strong "a priori" grounds for assuming that the causal organism of the two diseases is identical.

If the difference in the symptoms between small-pox and cow-pox be advanced as a reason for their being caused by different organisms, the answer is that naturally the symptoms are different for we have altered one of the principal factors of the experiment. we have substituted for the human species the bovine species; and there is ample evidence showing that the symptoms produced by a pathogenic organism in one species of animal vary considerably from those produced by the same organism in another species.

We must therefore conclude, either that the one is a modified form of the other, or that the relationship between small-pox and vaccinia is opposed to that of all other diseases known to medical science. It is surely unreasonable to adopt the latter conclusion except under the most positive proof; this, not only, is not available, but the weight of evidence is even against it.

An argument usually brought forward against the identity of the organisms is that numerous inoculations of bovines with variolous matter from cases of small-pox in man have failed to produce cow-pox. For these failures there occurs to me the following obvious scientific explanation, which, however, I have not before seen stated. Cow-pox, compared with small-pox, is a very mild disease. Granted for purposes of argument that small-pox and cow-pox are caused by the same organism, this mildness of the disease may be accounted for by the theory that bovines, as a species, are only slightly susceptible to this organism. (There is no doubt that in bovines the organism of small-pox becomes modified, and to this modified form of course they are readily susceptible, for there is no difficulty in transmitting cow-pox from generation to generation of calves.) If therefore as a species bovines



are only slightly susceptible, it is reasonable to suppose that the majority will be totally insusceptible, and that only here and there will be found an individual in which natural immunity is not so complete; hence a number of trials may need to be made before one of these susceptible individuals is happened upon. It is recognised that amongst human beings there are many who are naturally immune to small-pox; this was demonstrated in the days of inoculation. If then we suppose an experimenter, in every case in which he tried to inoculate the disease had, by some chance, selected only those naturally immune, he would have fallen into the error of supposing that human beings were naturally immune to small-pox. How much more readily therefore will an investigator fall into error from the inoculation of variolous matter into the bovine species in which it is the rule for natural immunity to be present, and the exception for a susceptible individual to be found.

This explanation appears to me to be perfectly reasonable and certainly accounts for the failures to produce cow-pox by the inoculation of variolous material that have occurred.

Still, without any such hypothesis, and admitting

the numerous failures, there are recorded many attempts of successful inoculation. If these are reliable they must necessarily override experiments with negative results.

There are on record the following successful attempts at the production of cow-pox in bovines by the inoculation of the variolous matter of small-pox:-

"Gassner of Gunsburg, in 1801;

"Viborg of Copenhagen, in 1807;

"Basil Thiele of Kasan, in 1836 and 1838;

"Ceely, in 1839, on two occasions;

"Badcock of Brighton, from 1840, 37 inoculations;

"Adams and Putnam, Boston, U.S.A., in 1852;

"Simpson in 1885, and in Calcutta in 1892;

"Fischer at Karlsruhe, in 1886 and 1890;

"Surgeon-Major King at Madras in 1889;

"Hime, in 1892;

"Haccius and Eternod, in Lancy, Geneva, 1893, on seven occasions;

Klein, in 1892; and

"Copeman in 1892." x

Here then is a list of successful experiments which cannot be ignored, and which must carry more weight than any number of unsuccessful attempts. It

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x "Vaccination", S.M. Copeman, Chap. 11.

is incredible that all these investigators either misrepresented their results, or were guilty of such carelessness or negligence in their experiments as to invalidate their conclusions.

For these and the foregoing reasons therefore there seems to me no possible doubt but that the causal organism of small-pox is identical with that of vaccinia.

Varicella

*Discuti (severe)*

*Notes of Case.*

Name { George  
Harry

Age 44

Diet milk

Case Book N.º





# DISEASE.

Varicella

Disinfect.

Notes of Case.

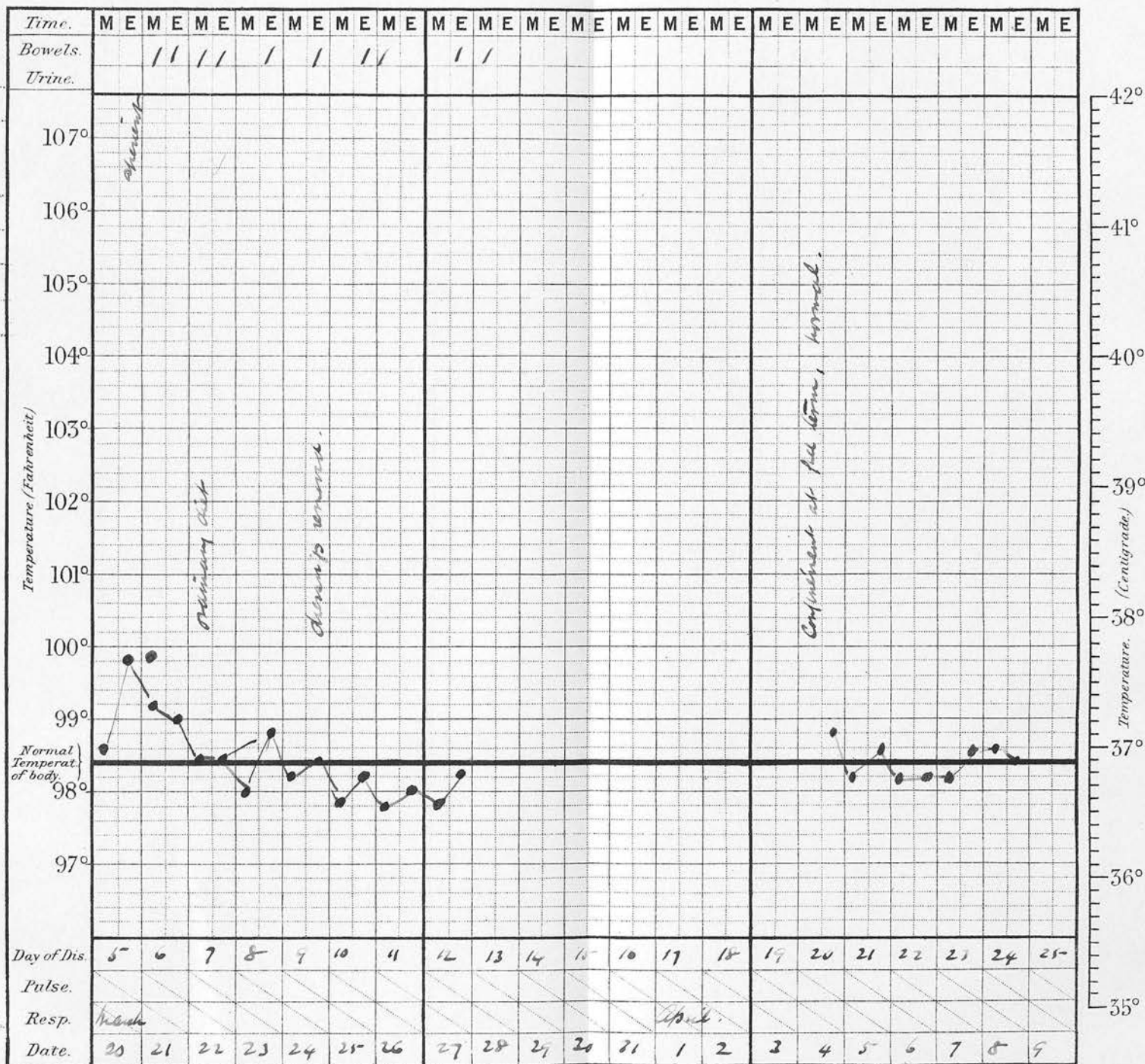
George

Name { Alie

Age 12

Diet milk

Case Book N<sup>o</sup>



Date of admission.

March 20-1902

Result Recovery.





[illegible]

Gould's Clinical Chart

## DISEASE.

Varicella

Confluent-

*Notes of Case.*

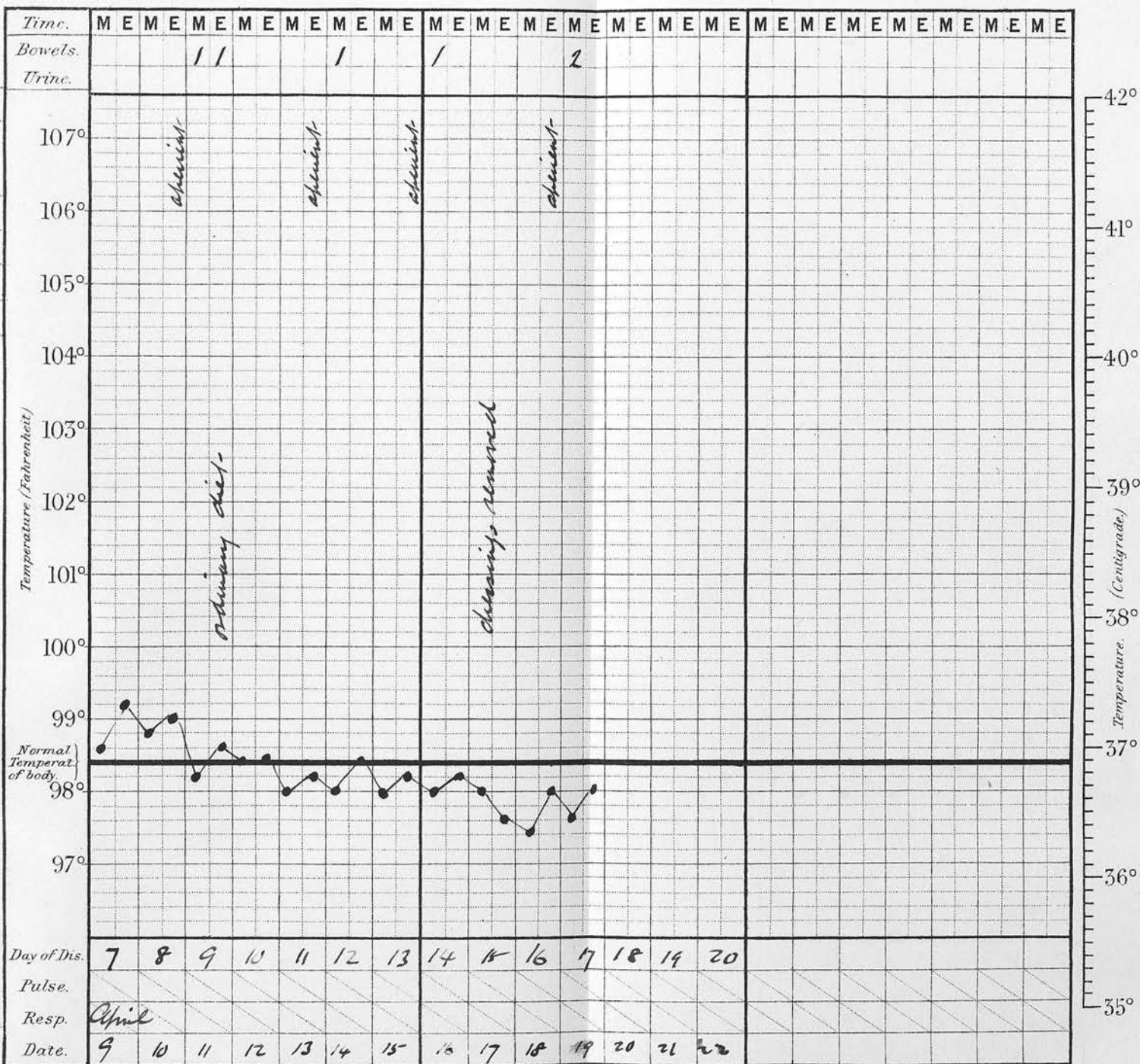
Turner

Name Harry

Age.....19

Diet ..... milk

Case Book N.º



*Date of admission.*

April 9<sup>th</sup> 1952

Result moving